

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method of selecting a polypeptide that is internalized into a target cell, said method comprising:

- B2
- i) contacting one or more target cells with one or more members of a phage display library displaying one or more polypeptides;
 - ii) washing said target cells to remove and eliminate ~~removing and eliminating~~ members of said library that are bound to the exterior surface of said target cells, wherein said washing comprises washing said target cells with a strong wash;
 - iii) culturing said target cells under conditions where members of said phage display library bound to an internalizing marker can be internalized; and
 - ~~iii~~iv) identifying internalized members of said phage display library that are internalized into one or more of said target cells, where said internalized members of said phage display library each display a polypeptide that is internalized into a target cell.

2. (Original) The method of claim 1, wherein said phage display library is an antibody phage display library.

3. (Original) The method of claim 2, wherein said antibody phage display library displays single chain antibody Fv regions.

B3

4. (Currently Amended) The method of claim 1, wherein said identifying comprises recovering internalized phage and repeating steps (i) through ~~(iii)~~(iv) to further select for internalizing binding moieties.

5. (Original) The method of claim 4, wherein said recovering comprises:

- (a) lysing said target cells to release internalized phage; and
- (b) infecting a bacterial host with said internalized phage to produce phage for a subsequent round of selection.

6. (Original) The method of claim 4, wherein said recovering comprises recovering nucleic acids encoding the phage-displayed antibody.

7. (Previously Amended) The method of claim 1, wherein said identifying comprises detecting expression of a reporter gene or a selectable marker.

B4 8. (Currently Amended) The method of claim ~~4~~51, wherein said cells of a subtractive cell line are present in at least 2-fold excess over said target cells.

9. (Original) The method of claim 1, wherein said target cells form an adherent layer in said method.

10. (Original) The method of claim 1, wherein step (ii) is performed at a temperature lower than step (iv).

B5 11. (Currently Amended) The method of claim 1, wherein step (ii) ~~is~~ comprises a wash performed at about 4°C.

12. (Original) The method of claim 1, wherein said phage express a selectable marker.

13. (Original) The method of claim 12, wherein said selectable marker is selected from the group consisting of a fluorescent protein, an antibiotic resistance gene, and a chromagenic gene.

14. (Original) The library of claim 13, wherein said chromagenic gene is selected from the group consisting of horse radish peroxidase, β -lactamase, luciferase, and β -galactosidase.

15. (Original) The method of claim 1, wherein said target cells are selected from the group consisting of solid tumor cells, members of a cDNA expression library, cells that overexpress a cytokine receptor, cells that overexpress a growth factor receptor, metastatic cells, cells of a transformed cell line, cells transformed with a gene or cDNA encoding a specific surface target receptor, and neoplastic cells derived from outside a solid tumor.

B6 16. (Currently Amended) The method of claim ~~4~~51, wherein said cells of a subtractive cell line are selected from the same tissue type as the target cells.

17. (Currently Amended) The method of claim ~~4~~51, wherein said cells of a subtractive cell line are selected from the group consisting of fibroblasts, monocytes, stem cells, and lymphocytes.

51. (Previously Added) The method of claim 1, wherein said method further comprises contacting the target cells with cells of a subtractive cell line.

52. (Previously Added) The method of claim 51, wherein said method further comprises contacting the target cells with live cells of a subtractive cell line.

53. (Previously Added) The method of claim 1, wherein said removing comprises contacting the target cells with a low pH wash.

54. (Previously Added) The method of claim 51, wherein said removing comprises contacting the target cells with a low pH wash.

55. (Previously Added) The method of claim 1, wherein said removing comprises contacting the target cells with a trypsin.

56. (Previously Added) The method of claim 51, wherein said removing comprises contacting the target cells with a trypsin.

57. (Previously Added) The method of claim 51, wherein the target cells are cells that are transformed a nucleic acid that encodes and expresses a target receptor and the subtractive cell line is the non-transformed cell line.

REMARKS

Status of the Claims.

Claims 1-17, and 51-57, are pending with entry of this amendment, no claims being cancelled and no claims being added herein. Claims 1, 4, 8, 11, 16, and 17 are amended herein. These amendments introduce no new matter. Support is replete throughout the specification and particularly in the claims as originally filed. The amendment to the specification corrects a typographical error. The amendment to claims 4, 8, 11, 16, and 17 are made for purposes of clarity and do not alter the